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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,291	12/04/2003	Stephen F. Badylak	3220-73986	7088

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EXAMINER	
FORD, ALLISON M	
ART UNIT	**PAPER NUMBER**
1651	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,291	BADYLAK ET AL.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-8 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending in the current application, all of which have been considered on the merits.

Priority

Applicant's claim for priority under 35 USC 119(e) to provisional application 60/431,091, filed 4 December 2002, and to provisional application 60/444,092, filed 31 January 2003, are acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are directed to a method of inducing repair of damaged or diseased liver tissue in a patient in need thereof, comprising administering to the patient a graft composition comprising basement membrane tissue of a warm-blooded vertebrate in an amount effective to induce repair of the liver tissue at the site of administration of the graft composition.

Claim 1 is considered indefinite because of the recitation of the term "basement membrane tissue." By definition a tissue is "**(tissue: 3:)** an aggregate of cells usually of a particular kind together with their intercellular substance that form one of the structural materials of a plant or an animal" (Merriam-Webster Online Dictionary, retrieved 12 September 2007), because basement membrane, per se, is acellular it is not appropriately called a tissue. Furthermore, in dependent claims the "tissue" is

required to be provided in a fluid, gel or powder, none of which could comprise a whole "tissue". It appears claim 1 should refer to a basement membrane *of* tissue, examination has been conducted as such.

Claims 1-8 are further rejected under 35 U.S.C. 112, second paragraph, for failing to correlate in scope with the specification. The specification repeatedly emphasizes the necessity of the removal of cellular components from the basement membrane material prior to use in a graft composition in order to avoid immunorejection upon implantation (See, for example, paragraph bridging pages 3-4 of the specification); however, the claims fail to require the basement membrane of a tissue to be devoid of endogenous cellular components of said tissue. Therefore there is an incongruity between the claims and the specification which renders the claims indefinite.

Claim 8 is further rejected as being of improper dependent form for failing to further limit the subject matter of previous claim 6. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. It is not clear how a multilayered homolaminate graft composition (claim 8) differs from a multilayered graft composition formed of two or more layers (claim 6)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the

specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to a method of inducing repair of damaged or diseased liver tissue in a patient in need thereof, comprising administering to the patient a graft composition comprising basement membrane *of a* tissue of a warm-blooded vertebrate.

Claims 1-5 are generic to the type of tissue the basement membrane is derived from, and thus are claiming methods of treatment involving administration of graft compositions comprising basement membrane from all types of tissue. Applicants are not considered to have sufficient written description to show they had possession of basement membrane from all types of tissue, but rather only show possession of basement membrane from liver tissue only, and thus the claimed method should be limited in scope to methods involving administration of graft compositions comprising basement membrane from liver tissue, only.

The specification is limited to discussion of basement membrane from liver tissue, how to obtain such material from liver tissue and how to use such in production of a graft for implantation to treat damaged or diseased liver tissue. The single species of liver tissue is not considered representative of the full scope of tissues from which basement membrane may be obtained, and thus Applicants fail to show they had possession of the full scope of the claims. Therefore the claims fail to fulfill the written description requirement.

Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for inducing repair of damaged or diseased liver tissue by administering a graft composition comprising basement membrane of liver tissue which is devoid of endogenous cells from said liver tissue, does not reasonably provide enablement for inducing repair of damaged or diseased liver tissue by administering a graft composition comprising basement membrane from any tissue type,

wherein the basement membrane may contain cells endogenous to said tissue type. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to carry out the inventive method commensurate in scope with these claims.

The instant claims are directed to a method of inducing repair of damaged or diseased liver tissue in a patient in need thereof, comprising administering to the patient a graft composition comprising basement membrane *of a* tissue of a warm-blooded vertebrate.

The showing in the specification is limited to methods involving administration of graft compositions comprising liver basement membranes, wherein the liver basement membrane is devoid of cells endogenous to the liver tissue. While the specification provides guidance and teachings on how to obtain basement membrane from liver tissues and how to remove cells from that specific liver tissue, there are no teachings or guidance for obtaining basement membrane from any other tissue types. Additionally there is not even a suggestion that the methods for derivation of liver basement membrane would be applicable to any tissue type; therefore one of ordinary skill in the art in reading the instant specification would have no reasonable expectation that such methods would be suitable for any tissue type.

Additionally, the instant specification stresses that removal of cellular components from the liver extracellular matrix is necessary for successful use of the graft material, as it renders the graft composition non-immunogenic and permits for penetration of the host's cells upon implantation (See, for example, paragraph spanning pages 3-4 of specification). If graft compositions comprising basement membrane as well as endogenous tissue and cells (i.e. basement membrane not fully separated from original tissue or still retains adherent native cells) were implanted in the instant method use of immunosuppressant drugs would appear to be necessary. Development of appropriate immunotolerance regimes would be considered undue experimentation. Therefore, it appears success of the instantly

claimed method requires use of liver basement membrane which is devoid of cells endogenous to the liver tissue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being obvious over Badylak WO 98/25637 and over Badylak US Patent 6,793,939 (national stage entry of PCT/US97/22727).

It is noted the applied **patent** reference (US 6,793,939) has a common inventor and assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2). Please note the WIPO publication is prior art under 35 USC 102(b) and cannot be overcome in such a manner.

Badylak discloses methods of inducing endogenous tissue formation at a site in need thereof by administering a graft composition comprising liver basement membrane in an amount effective to induce the repair of the liver tissue at the site of administration. Badylak disclose the graft composition can be administered as a multilayered composition formed from two or more layers of liver basement membrane (See WO 98/25637 Pgs 8-9/ See USP '939 col. 6, ln 13-64). The thickness of individual layers/sheets would be routinely optimized to suit the intended implantation site's needs (size and shape). Badylak further state the basement membrane can be provided in various forms, including a fluidized liquid (which can also be considered a gel) or powder form (See WO 98/25637 Pg. 4-5/ See USP '939 col. 3, ln 45-col. 4, ln 11).

While Badylak state the graft composition can be administered to any endogenous tissue site in need of repair, he does not specifically disclose the liver as an implantation site. However, at the time the invention was made the need for a method of repair and/or regenerating liver tissue was well recognized, and thus the artisan of ordinary skill would have good reason to pursue treatment of the liver via the general method disclosed by Badylak. There would be a reasonable expectation that treatment of damaged liver would be successfully accomplished by the method of Badylak because the graft composition of Badylak contains basement membrane derived from liver tissue and Badylak suggests the material would support hepatocyte growth (See WO/ 98/25637 Pg. 12/ USP' 939, col. 8, ln 55-65). Therefore, it would have been obvious to the person of ordinary skill in the art to try to specifically repair liver tissue as the endogenous tissue site for repair a reasonable expectation that the composition would be suitable for use in liver tissue repair because such was a known option with a recognized need, and such a method would be within the technical grasp of the artisan. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-8 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,793,939. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are directed to inducing formation of tissue in a subject in need thereof by implanting the same graft composition. The difference between the patented claims and the instant claims is that the patented claims are generic to repair of any endogenous tissue type, whereas the instant claims are specifically to repair of liver tissue. However, at the time the invention was made the need for a method of repair and/or regenerating liver tissue was well recognized, and thus the artisan of ordinary skill would have good reason to pursue treatment of the liver via the general method disclosed by Badylak. There would be a reasonable expectation that treatment of damaged liver would be successfully accomplished by the method of Badylak because the graft composition of Badylak contains basement membrane derived from liver tissue and Badylak suggests the material would support hepatocyte growth (See Badylak, col. 8, ln 55-65). Therefore, it would have been obvious to the person of ordinary skill in the art to try to specifically repair liver tissue as the endogenous tissue site for repair a reasonable expectation that the composition would be suitable for use in liver

tissue repair because such was a known option with a recognized need, and such a method would be within the technical grasp of the artisan.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651